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Psychophysiological Measures and Methods in Trauma Research

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As the importance of physiological aspects of posttraumatic stress disorder (PTSD) becomes more evident, many researchers are interested in measuring physiological variables in their PTSD studies. But even for those with the requisite expertise in psychophysiology, the special technical and methodological considerations of this kind of research make it daunting. Fortunately, relatively "low-tech" psychophysiological measures can yield valuable results in the study of PTSD, and the necessary technology is increasingly available to medical and psychological researchers. In this chapter, we will review recent PTSD research on peripheral sympathetic nervous system variables and describe a number of technical and methodological considerations that are relevant to such studies. Finally, we will briefly review research on additional psychophysiological variables and discuss the directions we expect research in this area to be taking in the future.

It has long been recognized that alterations in physiological responsivity are associated with exposure to traumatic stress. Terms such as Soldier's Irritable Heart, which was applied to veterans of the American Civil War, captured the syndrome of increased heart rate and blood pressure responsiveness to reminders of the original trauma. At the time it was thought that the stress of war was associated with an impairment of cardiac function which led to these symptoms, which are now included in the reexperiencing cluster for the DSM-IV diagnosis of posttraumatic stress disorder. Later, Freud thought of combat-

related psychopathology as being related to conflicts over whether or not to run from the battlefield. His influence led to a general understanding of physiological reactivity to trauma as an expression of an unresolved conflict. With the First and Second World Wars came a renewed interest in a possible direct physiological basis for the enduring symptoms associated with the psychological trauma of combat. Kardiner (1941) advanced the hypothesis that excessive sympathetic activity was responsible for symptoms such as increased physiological responsiveness to reminders of the original trauma.

Since the time of the Second World War the psychophysiology paradigm has been widely applied in the study of the sympathetic nervous system in patients with PTSD. Kolb (1984) has pointed out that many of the symptoms of PTSD, including sleep disturbance, hypervigilance, physiological arousal, and exaggerated startle response, could possibly be related to alterations of sympathetic systems. He described the phenomenon of increased physiological reactivity to reminders of the original trauma as a "conditioned emotional response." In principle, this response can be studied in controlled conditions in the laboratory using psychophysiological techniques.

The typical psychophysiological challenge paradigm involves the measurement of physiological signals at rest and during exposure to reminders of a previously experienced traumatic event. Bioelectrical signals generated from the body are conducted by surface electrodes and transducers. The signals are then filtered, amplified, and recorded for later interpretation of their biological or psychological significance. Physiological variables most often examined in relation to PTSD include heart rate, systolic and diastolic blood pressure, skin conductance, and electromyographic (EMG) activity of the frontalis, corrugator, zygomaticus or orbicularis oculi muscles. These variables reflect, in part, activity of the peripheral sympathetic nervous system. This system is activated during the stress response, in addition to being linked to central catecholaminergic systems which play an important role in mobilization in response to stress.

The procedure generally begins with a baseline rest period followed by exposure to trauma-related and neutral cues. The format of trauma reminders utilized in the psychophysiology paradigm has included slides (with or without accompanying sounds) that depict the general type of trauma (e.g., combat), and imagery scripts, which are descriptions of the traumatic experiences from the perspective of the affected individual. Comparisons are then made between reactions to trauma-related material and either baseline levels or reactions to neutral material. The use of slides and sound tracks has the advantage of being consistent from one subject to the next, while the script technique has the advantage of being more specific to the individual's traumatic experience. Psychophysiological responses, in general, have the advantage of being direct measures of a construct which is felt to be a central component of PTSD.

Prins, Kaloupek, and Keane (1995) recently reviewed the evidence relating psychophysiological variables to PTSD diagnosis and concluded that there is strong support for the hypothesis that individuals with PTSD show greater autonomic reactions when they are exposed to trauma-related stimuli than do individuals without PTSD. In addition, they noted that there are often differences in baseline levels of autonomic activity between groups differing with respect to PTSD (e.g., Blanchard et al., 1982; Pallmeyer et al.,1986; Pitman et al., 1987; Gerardi et al., 1989). These differences in baseline levels appear to be an example of autonomic elevation due to subjects' anticipation of trauma-related presentations in later portions of the protocol. This is a potentially important distinction because it means that the higher physiological readings (e.g., for heart rate) are not due to a biologically stable elevation in autonomic activation but instead are the result of entering a potentially threatening situation.

Prins et al. (1995) note that the strongest evidence for physiological differentiation of PTSD is found in relation to combat-related trauma, and the most consistent indicator is heart rate. Combat veterans with PTSD show significantly more heart rate reactivity to combat stimuli than various comparison groups (i.e., normal controls, non-veterans with other psychiatric diagnoses, combat veterans with no mental disorder) across protocols that have utilized standardized audio or audio-visual combat stimuli (Blanchard et al., 1982; Pallmeyer et al., 1986; Blanchard et al., 1986; Gerardi et al., 1989; Blanchard et al., 1989; Malloy et al., 1983; Pitman et al., 1987; McFall et al., 1990; Pitman et al., 1990; Orr et al., 1993; Shalev et al., 1993). Significant differences are also evident with respect to skin conductance, and they were most clear when the idiographic imagery procedure was used. Finally in terms of subjective distress, Vietnam veterans with PTSD consistently report more distress to combat material than do Vietnam veterans without PTSD, regardless of the psychophysiological assessment format used.

Despite the frequent replication of differential psychophysiological response by PTSD subjects to trauma cues, including demonstrations with traumatized populations other than combat veterans (e.g., Shalev, Orr, & Pitman, 1993; Blanchard, Hickling, Taylor, Loos, & Gerardi, 1994), as many as 40% of patients with PTSD do not show the expected differential reactivity. In fact, Prins et al. (1995) highlight a general trend across studies that indicates better performance by psychophysiological assessment in identifying individuals who do not qualify for an interview-based PTSD diagnosis than in identifying those who do qualify for the diagnosis. There are several possible reasons for this limited accuracy, some of which are addressed in the following sections concerning misconceptions about psychophysiology, factors that need to be considered when planning for psychophysiological protocols, and factors that reduce assessment accuracy.

Psychophysiological Measures: Common Misconceptions

Psychophysiological measures can provide converging evidence for diagnosis, index hyperarousal and reactivity in a manner that doesn't rely on self-report, and supply quantitative information for evaluating treatment effectiveness. These considerations can provide strong justification for the cost and effort of using physiological measures. On the other hand, psychophysiological assessment sometimes has an exaggerated image as a truly objective means for detecting an individual's psychological state. This and other common misconceptions about psychophysiological methods need to be dispelled as a first step in understanding their value.

Misconception #1. Psychophysiological measures are objective, immune to faking, and capable of providing a direct window on the true psychological state of an individual. While these methods can provide unique information, they are not inherently more valid nor more objective than typical assessment methods involving self-report or interviews. In addition, psychophysiological assessment is subject to ambiguous outcomes just like any other assessment method. In clinical application, findings often aren't fully consistent with a PTSD diagnosis (or absence of such). Insofar as faking is concerned, there is limited evidence on the issue in the context of PTSD. Gerardi, Blanchard, and Kolb (1989) suggest that veterans with PTSD have modest ability to suppress responding, but many of those without PTSD can increase responding purposely. Given this evidence, it is important to realize that all of the current challenge protocols (i.e., involving presentation of trauma-relevant depictions) require some degree of active cooperation by the individual being assessed. The ability to shift attention, imagine other scenes, and generate physical movements that affect physiological reactions are all options which, if exercised selectively, would have the potential to allow dissimulation.

Misconception #2. Psychophysiological measures are relatively interchangeable as indicators of arousal. There is ample evidence that measures are differentially sensitive to emotional and psychological states and behaviors. Fowles (1980) in particular has explored some of the differential value of heart rate and skin conductance as psychophysiological indicators. As a simple example, it appears that heart rate will better index responding associated with active avoidance behavior, while skin conductance will better index active inhibition. Thus, the fact that a measure can be conceptualized as psychophysiological in nature does not guarantee that it will be appropriate for the application in question. Conversely, it should be noted that the concept of arousal is itself problematic because it implies a sort of unidimensional energy underlying all emotion, cognition, and behavior. This overly simplified perspective can lead to inappropriate interpretation and cross-study mixing of evidence. It is important to instead think in terms of the state to be indexed and the underlying autonomic activity that is expected to couple to this state most closely.

Misconception #3. There is a constant reciprocal relationship between sympathetic and parasympathetic activity in the autonomic nervous system. It is commonly taught that the fight or flight (sympathetic) and inhibitory (parasympathetic) branches of the autonomic nervous system have a fixed relationship. When activity is high in one, it is necessarily low in the other. This is quite incorrect. These two subsystems have independent and complimentary effects, as well as their better known reciprocal effects (Berntson, Cacioppo, & Quigley, 1991). This is an important distinction because it affects the selection of measures and the interpretation of findings. For example, it cannot be assumed that an increase in heart rate is uniquely due to increased sympathetic activity. It could be the result of at least three patterns of activation: 1) sympathetic activation, 2) parasympathetic withdrawal, or 3) concurrent activation in both subsystems, which might be dominated by sympathetic effects. Psychophysiological studies of PTSD have not addressed this distinction thus far, but future efforts will perhaps do better in this regard.

Planning for a Trauma-Oriented Psychophysiology Lab

The first step in planning for a new lab or the upgrade of an existing lab is to outline and prioritize the uses it will be expected to serve. Considerations that need to be taken into account include the aims of the recording, the range of measures to be examined, the level of flexibility required in setup, the relative ease of use, capacity for data storage and manipulation, and the environment in which measurements will occur. Some concrete questions in relation to each of these considerations are listed below.

Aims of Recording

Is the recording primarily for clinical or research purposes or both? In some respects this is becoming a false distinction as managed care and other influences increase the need for careful, systematic recording in the clinical setting. Nonetheless, the particulars of the clinical or research application(s) in question will determine what the equipment must be able to do.

Range of Measures

Heart rate and skin conductance are the most typical measures in the literature to this point. Do you require others? Are you willing to use back or chest leads to get a stable heart rate signal, or will other less intrusive attachments (e.g., limb leads or photoreflective finger clip) be preferable despite the problems with signal loss that may occur? How much time are you willing or able to spend with preparation and attachments for each recording session? The time required for setup can range from 1–2 minutes to 10 minutes or more, depending on number and type of measures.

Level of Flexibility

Will the equipment be dedicated to a single protocol or modified for different protocols as they arise over time? The advantages to having a dedicated function for lab equipment extend all the way from the planning stage through implementation and long-term use. For example, it is easier to specify the precise equipment features that the protocol requires, training of technicians can be simplified, and there is less likelihood of inadvertent loss of recordings due to incorrect setup. This latter problem often arises when equipment is used for multiple purposes that require different configurations or settings. Checklists can be used to verify proper setup, but mistakes still occur. On the other hand, it may not be practical or economical to limit use to a single protocol, and the ability to adapt to different applications may be one of the factors that recommend one brand or model of equipment over another. Whatever the situation, it can be anticipated that, in general, more flexible equipment will be more technically complex to use.

Ease of Use

What level of technical support will be available both initially during implementation and later during extended use? It is important that even the simplest recordings are subject to scrutiny by someone with technical familiarity with the equipment and the indices in question. Expert guidance should be sought from the perspectives of safety, as well as reliability, and validity of measurement. Likewise, it can be advantageous to have some staff devoted to the recording process so that training can be detailed and procedures have greater likelihood of being applied systematically. Will non-technical staff (e.g., clinical care providers) be expected to conduct their own recordings? If so, ease of use will be one of the foremost considerations.

Data Storage and Manipulation

What will be done with the recordings? Will they merely be displayed back in real-time for the purposes of biofeedback, or will some retention and processing be in order? While there may be some modest applications for which data retention isn't worthwhile, it is probably a good idea to purchase equipment with some built-in or accessory means of data storage. Certainly any research application will require this capacity. Even in the clinical realm, however, it is increasingly important to have data on hand as documentation of assessment or treatment efforts.

The Recording Environment

Will the recording always be done in one place or will it need to be portable so that it can move from room to room? Will it be desirable, or possible, to conceal the equipment from view? Will recording need to allow for physical movement either in a relatively confined space or in the real-world environment? Reasonably good quality equipment is available for applications that range from ambulatory recording through portable recording that can be moved readily from room to room, to stationary recording restricted to one setting. The advantages of portability should be weighed carefully against the challenges it creates. Ambulatory recording can be highly idiographic and may have very direct relevance to the problems in behavior, emotion, or functioning that a person reports. However, it can be a substantial challenge to summarize the volume of data that often results, and there are a number of uncontrolled influences on physiological systems (e.g., activity or speaking) that complicate the scoring and interpretation of data. Both ambulatory and portable equipment have increased opportunity for damage due to accidents and misuse. Bumps and jars can also cause more subtle problems by affecting calibration settings. Portable equipment also may be used in a variety of physical environments where factors such as temperature, humidity, noise, seating comfort, and visual clutter vary and introduce error into the measurement process. By contrast, despite the loss of flexibility, an identified recording space can be prepared to serve its purpose optimally and to do so systematically for all recording sessions.

The Need for Consultation

The critical second step in planning for psychophysiological measurement is to arrange for expert consultation. It is not the first step only because it is important to think through some of the previously listed considerations before contacting the potential consultant. Even if there are many uncertainties remaining after you proceed as far as you can on your own, you should at least be able to show initiative by taking responsibility for the effort. This approach also makes it much easier to discuss what it is that you need in the way of consultation services. Such preparation will be viewed quite positively by potential consultants who might otherwise be reluctant to become involved with a project where the need for assistance appears too great. Initiative on your part gives a sense of active involvement which is both warranted and wise in your quest for a good consultant.

Sample Psychophysiological Paradigms

The choice of procedures for a psychophysiological protocol depends on the purpose and aim of the study. The most common use thus far has been with traumatized individuals for diagnostic purposes (Keane et al., 1987). An example of one protocol which could be used for a diagnostic screening for combat-related PTSD is as follows:

0–5 min.	Resting baseline followed by Subjective Units of Distress Scale (SUDS) ratings.
5–11 min.	Six one-minute presentations of neutral slides and accompanying music soundtrack, each followed by a SUDS rating.
11–16 min.	Resting baseline followed by SUDS ratings.

16–22 min.	Six one-minute combat slides and accompanying combat sounds soundtrack, each followed by a SUDS rating.
22–27 min.	Recovery period followed by a SUDS ratings.

Rule of thumb criteria that might be used as indicators of psychophysiological reactivity: 1) a 5 beats per min. greater heart rate maximum during the combat slide presentation when compared to the neutral slide presentation, and; 2) a greater than 50 point difference in SUDS scores between the highest rating for a combat slide presentation compared with the highest rating for a neutral slide presentation. Although the example only includes heart rate, in general, use of more physiological measures that indicate differential reactivity to the trauma cues increase confidence in the diagnostic interpretation.

The acoustic startle paradigm provides another noninvasive measure of the physiological correlates of PTSD, although the diagnostic relevance of this index has not been determined. Increased eyeblink startle magnitude has been found in Vietnam combat veterans with PTSD in comparison to Vietnam combat veterans without PTSD with 80-100 dB noise bursts (Pallmeyer et al., 1986; Butler et al., 1990). An increase in heart rate and skin conductance during the startle paradigm has also been reported in patients with civilian PTSD in comparison to controls (Shalev et al., 1992). Not all studies have produced positive findings, however (Paige et al., 1990; Ross et al., 1989). Startle testing requires the development of a laboratory for the delivery of sound bursts at specific decibel ranges in a controlled environment, with the capacity for measurement of the oculomotor reflex. Consultation with an experienced startle investigator is advisable before attempting studies of this type.

Factors That Can Reduce the Accuracy of Psychophysiological Assessment

Task Compliance

One of the most basic considerations, but one which is too easily overlooked, is the need to maximize compliance with the assessment task.

This means, for example, maximizing compliance with instructions to sit quietly and rest, to view audiovisual presentations, or to make ratings of distress at the appropriate time. More subtle factors come into play as well because of the emotionally-evocative nature of the material being presented. It may be very difficult for those being tested to stay engaged with a task that causes them distress. They may try to limit distress by turning away, distracting themselves, or focusing artificially on some mundane feature of the display. They may also self-regulate physiological responding by using physical maneuvers (e.g., deep breathing) that dampen autonomic response. Conversely, because motor activity can itself elevate physiological activity, fidgeting and other such extraneous movements during the procedure can increase reactivity.

Many of these factors can be mitigated by careful planning of the phrasing and delivery of instructions. However, some of the factors are substantially beyond the ability of the clinical investigator to compel or control. For example, it would be unethical to arrange the presentation of trauma-related material in such a way that the individual could not readily escape or terminate the procedure. The best alternative then becomes a matter of documenting any significant violations of the protocol. Recordings of eye movements and closures, large muscle movements, and respiration are among the types of auxiliary physiological measures that might be used to identify departures from the protocol. This information, in turn, can be used as a basis for eliminating or adjusting intervals during which formal task compliance was in question.

The issue of compliance also can be viewed from a broader perspective that takes into account the clinical value of behavior exhibited during psychophysiological challenge procedures. Many of the compliance failures during psychophysiological testing are meaningful behavioral indicators of distress. The fact that someone is unable to view or attend to the trauma-related material can be as important clinically as the fact that someone else shows a larger heart rate reaction to trauma-related material than to neutral material. In the context of most clinical evaluations, the psychophysiological protocol offers the only opportunity to observe the individual as he or she typically functions

in the presence of trauma cues. It is a good idea to capitalize on this opportunity by having some means of unobtrusive observation during the test procedure. It is highly advantageous to follow the testing with a structured debriefing to question the individual in detail about self-protective or self-regulatory behavior used during testing. Not surprisingly, a number of things that are reported during the debriefing are sufficiently subtle or unobservable to escape detection by others. With the debriefing, it is almost always possible to collect clinically useful information of some type. Given that the aim is to collect meaningful physiological and behavioral information, a broad perspective on the procedures makes it likely that at least one or the other will result from testing and contribute to the clinical formulation.

Factors That Affect Physical State

One of the most basic considerations for psychophysiological measurement is physical comfort. Laboratory temperature or humidity should be sufficiently well controlled to not cause discomfort. Seating needs to be comfortable and to remain so for the duration of the testing period. Similarly, headphones or other attachments must be designed and adjusted so as to be well tolerated for the duration of their use. On a more basic level, one of the most disruptive, though readily preventable, discomforts is the full bladder. Routine bladder emptying is highly recommended in advance of any physiological testing.

Medications can also constitute a strong influence on physiological responding, particularly drugs with clear autonomic effects (e.g., beta blockers). In clinical settings, it is often not feasible to conduct psychophysiological testing on medication-free individuals. Unfortunately, the impact of many medications is either unknown or difficult to quantify at the individual level. Thus it is generally not possible to specify a dose-related formula for adjusting the responding of medicated individuals to estimate their unmedicated status. At minimum, however, it is a good idea to at least document the medication status of anyone who is tested so that its impact can be considered in the course of interpreting the physiological findings.

Nicotine and caffeine also can have a pronounced influence on physiological systems that are typically monitored in PTSD assessments. Unfortunately, their effects are not uniform across physiological systems and the impact of withdrawal can be as problematic as that due to consumption (e.g., Hughes, 1993; Lane & Williams, 1985; Lyvers & Miyata, 1993; Perkins, Epstein, Jennings, & Stiller, 1986; Ratliff-Crain, O'Keeffe, & Baum, 1989). The result of these complications is a common practice of requesting that individuals refrain from smoking or drinking caffeine for some period (often 30 minutes or more) prior to the psychophysiological assessment. This seems to be a reasonable step, though it is worth recognizing that some people may find the period of abstinence long enough to cause discomfort. Additionally, it is a good idea to question and document the person's usual daily intake (e.g., cups of caffeinated beverages, number of cigarettes), the amount consumed to that point on that day, and the actual amount of time since last intake. As with medications, there is no available means for translating this information into a formal adjustment, but it can be useful to the process of interpretation of findings.

Limitations of Physiological Measures

As noted earlier, there are no easily obtained, error-free measures of autonomic nervous system activity, let alone measures specific to the condition of PTSD. This consideration is compounded by the limited specificity that measures demonstrate with respect to important behavioral or psychological influences. For example, skin conductance responses are commonly observed when attention is drawn to a new stimulus regardless of content, as well as when a stimulus has threat value and elicits an emotion such as fear. It is therefore necessary to rely on convergence of measures, both physiological and nonphysiological, to develop a picture of the disorder. This sort of construct-oriented approach is further aided by careful planning of tasks and selection of measures. The aim is to reduce the likelihood of multiple influences and alternative explanations for an observed pattern of findings.

In this context, it is highly advisable to include a resting baseline period prior to any significant psychophysiological data collection, and to have a set recovery period after the task is complete. Recommendations about baseline length (e.g., Hastrup, 1986) point to a minimum

of 10 to 15 minutes for studies that examine psychophysiology in relation to acute laboratory stressors. Recovery periods of 5 to 10 minutes are probably sufficient. Recordings from these periods can provide critical context for interpretation of data. A concrete (and fairly common) example of their importance is the case where someone shows fairly high physiological activity throughout a diagnostic assessment procedure, including initial baseline, and then shows a substantial decrease in activity during recovery. This pattern suggests that the absence of differential response across sections of the procedure (e.g., neutral vs. trauma-related presentations) is due to a high level of anticipatory responding. Such anticipation can be sufficiently strong to elevate responding during reference periods and to preclude differences between baseline and reference periods. If this hypothesis is supported by other information (e.g., from observation or a debriefing interview), it favors interpretation of the evidence as consistent with PTSD. In contrast, simple comparison between neutral and trauma presentation periods in this example without consideration of the baseline and recovery would lead to a presumably incorrect conclusion that the evidence is inconsistent with a PTSD diagnosis.

Limitations Associated with Using Physiological Measures to Make a Diagnosis

One problem associated with using physiological measures to make a diagnosis that the multiple symptom options available under the diagnosis of PTSD make it possible to obtain a diagnosis of PTSD without the presence of psychophysiological reactivity. The fact that reactivity per se is not required by the diagnostic criteria opens the way for heterogeneity among cases and makes it understandable that there might be a limited association between diagnosis and results of formal psychophysiological measures. Even apart from this source of variation, it is important to recognize that the foundation of the PTSD diagnosis is subjective information that isn't necessarily comparable to information recorded directly from physiological systems. For example, research on autonomic perception and response covariation (e.g., Eifert & Wilson, 1991; Spinhoven, Onstein, Sterk, & Haen-Versteijnen, 1993; Tyrer, Lee, & Alexander, 1980) makes it clear that self-reports of psychophysiological reactivity are not interchangeable with observations or recordings of such activity.

From another angle, it is clear that several forms of psychopathology often accompany PTSD, particularly depression, anxiety, and substance abuse (Davidson & Fairbank, 1993; Keane & Wolfe, 1990). Evidence from outside the trauma context suggests that these conditions can have independent impact on psychophysiological responding (e.g., Lahmeyer & Bellur, 1987; Sayette, Smith, Breiner, & Wilson, 1992; Storrie, Doerr, & Johnson, 1981) and thereby complicate the interpretation of physiological evidence. Some effort to quantify comorbid problems in these areas is, therefore, well justified when PTSD is the target of interest.

Individual Biological Influences

Without going into detail, it is clear that individual differences that can influence psychophysiological reactivity arise from subject characteristics such as age, sex, race, menstrual cycle, and physical fitness level. Their relationship to sustained and reactive features of autonomic activity have been established in studies employing psychophysiological methods, and quantification of this information is highly encouraged whenever such methods are applied. There are few examples from the trauma literature that directly demonstrate the impact of these factors; however, one study by Shalev et al. (1993) did find that female subjects with PTSD demonstrated 33% greater physiological responding to their trauma script than male subjects with PTSD. More examples like this can be expected as the literature on the psychophysiology of trauma develops.

Appropriateness of Trauma Cue Presentations

The final influence to be noted as a potential explanation for imperfect association between psychophysiological responding and PTSD diagnosis is cue adequacy. A question that must be asked each time a trauma-related psychophysiological challenge is administered is how well the challenge material matches the individual's traumatic event. In this respect there may be an advantage to idiographic approaches to

trauma cue selection. While standardized presentations benefit from uniformity and their potential for allowing tight experimental control, they suffer the disadvantage of variable degree of correspondence with individual experience. Idiographic presentations may be designed to closely approximate the internal (memory) representations of the traumatic experience and thereby improve the validity of assessment.

As a related point, Anderson and McNeilly (1991) have recently argued for a contextual approach to psychophysiological research. Basically, this involves viewing psychophysiological responding as a function of the ecological niche that the person inhabits at the time of assessment. It is important to consider the testing situation from the first-person perspective, to think about the meaning and potential sources of threat cues for traumatized individuals. This outlook will both help to improve the application of psychophysiological methods and increase the likelihood that the information obtained from all aspects of the procedure is of value to clinical care and scientific advancement.

Measurement of Other Physiological Variables in PTSD

Other methods have been utilized in the assessment of physiological corrrelates in PTSD. We briefly review below research methods which are more complicated to institute than the psychophysiology paradigm. These methods can provide important information about the neurobiology of PTSD.

Studies of neurotransmitter function have provided evidence for alterations in catecholaminergic function in PTSD which are consistent with findings from the psychophysiology literature. Increases in urinary norepinephrine and epinephrine have been found in PTSD patients in comparison to patients with other psychiatric disorders and healthy controls (Kosten et al., 1987; Mason et al., 1988). Other investigators, however, have found no difference in urinary levels of norepinephrine or cortisol in patients with PTSD in comparison to Vietnam veterans without PTSD (Pitman et al., 1990a), or in plasma levels of norepinephrine at baseline in Vietnam veterans with PTSD in comparison to healthy controls (McFall et al., 1992; Blanchard et al., 1991). An increase in plasma epinephrine (McFall et al., 1990) and norepinephrine (Blanchard et al., 1991) has been shown following exposure to traumatic reminders in Vietnam veterans with PTSD in comparison to healthy subjects. A decrease in platelet adrenergic $alpha_2$ receptor number, possibly secondary to high levels of circulating catecholamines, has been observed in PTSD patients in comparison to healthy controls (Perry et al., 1987). Although these studies do not consistently support an increase in basal sympathetic function in PTSD, they do suggest that patients with PTSD may have an increased responsiveness of the sympathoadrenal system.

Pharmacological studies are also consistent with alterations in noradrenergic function in patients with PTSD. The $alpha_2$ antagonist, yohimbine, blocks the noradrenergic presynaptic autoreceptor, resulting in an increase in firing of noradrenergic neurons and an increased release of norepinephrine in the brain. Yohimbine administration results in flashbacks in 40% and panic attacks in 70% of Vietnam veterans with combat-related PTSD, an increase in PTSD-specific symptomatology, increased MHPG, blood pressure, and heart rate response in patients with PTSD in comparison to normal healthy controls (Southwick et al., 1993).

Furthermore, we are currently studying Vietnam combat veterans with PTSD and healthy subjects using positron emission tomography (PET) and [^{18}F]2-fluoro-2-deoxyglucose (FDG) in the measurement of brain metabolism following administration of yohimbine or placebo. Brain metabolism correlates with neuronal activity, therefore PET measurement of metabolism is a good indicator of functional activity of the brain. We know from studies in animals that high levels of norepinephrine release in the brain will have the effect of reducing brain metabolism in the cerebral cortex, whereas lower levels of norepinephrine release in the brain may actually cause an increase in metabolism. We hypothesized that if PTSD is associated with an increase in sensitivity and an increase in norepinephrine release in the brain relative to controls following yohimbine challenge, that there would be a relative decrease in metabolism with yohimbine compared to controls. Consistent with this, we found that yohimbine administration is associated with

a relative decrease in metabolism in cerebral cortical areas in PTSD compared to controls, namely in temporal, parietal, prefrontal, and orbitofrontal cortex (Bremner et al., 1995).

Findings from psychophysiological studies are also of potential value for understanding alterations in memory function in patients with PTSD (van der Kolk et al., 1989; Charney et al., 1993; Bremner et al, 1993). Exposure to trauma-related slides and sounds or scripts of the individual's traumatic event often results in the recall of trauma-related memories and associated affect. The psychophysiology challenge paradigm offers a means for studying pathological traumatic recall, which is an important part of the symptomatology of PTSD.

As reviewed in greater detail elsewhere (Bremner et al., in press), pathological traumatic recall involves a variety of brain structures which are involved in memory and which are probably abnormal in patients with PTSD. The amygdala mediates the startle response and conditioned emotional responses to traumatic cues such as loud noises. The hippocampus plays an important role in short-term recall, and also is involved in conditioned responses to complex spatially-related cues. A decrease in volume of the right hippocampus (possibly related to neuronal damage secondary to high levels of glucocorticoids, which are associated with traumatic stress) with deficits in short-term verbal memory has also been associated with PTSD (Bremner et al., 1993b; Bremner et al., in press).

Future Directions for Psychophysiological Research

Psychophysiological research has provided a great deal of useful information for the study of PTSD. Psychophysiology studies have demonstrated a robust and reproducible increase in heart rate, skin conductance, and blood pressure with exposure to traumatic reminders with a variety of methodologies and patient populations. These increases also are seen at baseline, in anticipation of contact with such reminders. Future studies are needed to expand this evidence to topics of clinical relevance such as the relationship between alterations in memory function and psychophysiological responding in patients with PTSD. For example, brain blood flow and metabolic correlates of the increased physiological arousal seen during the paradigm could provide important information about brain correlates of pathological remembering in patients with PTSD. Psychophysiology as a predictor of treatment response, for both psychotherapy and psychopharmacology, should be explored as well (Solomon, Gerrity, & Muff, 1992). Finally, the psychophysiology paradigm could also be used to examine important trauma-related symptom areas such as dissociation. The relative noninvasiveness and increasing ease of use of psychophysiology equipment encourages wider application in these areas in years to come.

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